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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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WHITHAM, CURTIS & CHRISTOFFERSON, P.C.
11491 SUNSET HILLS ROAD
SUITE 340
RESTON, VA 20190

EXAMINER	
NGUYEN, BAO THUY L	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,156	OKADA ET AL.	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 13 December 2004 has been received. Claims 1-7 are pending.

Priority

2. Applicant's claim for priority to parent application number 09/120,192 is acknowledged.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kouvonen et al (US Patent No. 5,965,458) in view of Williams et al (US Patent No. 6,080,400) and Krivan et al (US Patent No. 5,512,282) for reasons of record, which are reiterated herein below.

Kouvonen discloses a test strip and method for rapid immunoassay of foodstuff for bacterial contaminants, for example. The test strip comprises a backing sheet and a receiving end pad and at a distance from a finishing end pad. A test membrane is provided between said pads. The membrane is intended for being brought into liquid flow contact with a sample. The test membrane preferably carries a test zone containing an immobile reagent and a control zone containing control substance. A label zone containing a mobile label is applied to the test membrane or into the absorbing pad at the receiving end, thus enabling the label to migrate to the test zone carried by liquid flow. The strip may also contain more than one test membrane in

the same strip in order to test different analytes, or the same membrane may contain more than one zone each containing different reagents. The strip may also contain several different concentrations of the same reagent or label, in order to determine different analyte concentrations semiquantitatively. See abstract and column 3 through 4. Kouvonen teaches latex or metal colloid as labels, and that the test strip can be adapted for many tests including assays of foodstuff. See column 5, lines 37-47 and column 8, lines 44-67. In one specific embodiment, Kouvonen teaches a method for the detection of occult blood in a fecal sample. Kouvonen teaches a test device designed for detection both human hemoglobin and human albumin. Hemoglobin is a more specific marker of blood which can occurs after intestinal bleeding in cancer patients, for example. See column 11, example 3.

Kouvonen differs from the instant invention in failing to teach the detection of verotoxin or verotoxin producing *Escherichia coli.*

Williams discloses that verotoxin producing *Escherichia coli* causes a life-threatening blood disorder that appears within 3 - 7 days following on set of diarrhea. Symptoms of hemolytic uremic syndrome (HUS) include renal glomerular damage, hemolytic anemia, thrombocytopenia, etc. Williams discloses that ingested organisms adhere to and colonize the intestinal mucosa, where toxins are released which causes endothelial cell damage and bloody diarrhea. Williams disclose a method for the detection of bacterial toxin by a sandwich assay utilizing antibodies directed against the bacterial toxin. Williams teaches that the immobilized antibody will be present in or on a solid support and exposed to a test sample and a reporter substance, which detects the presence of bound toxin. See column 4, lines 50-62; column 5, lines 20-65; and column 31, lines 4-40.

Krivan discloses that antibiotics are contraindicated in the treatment of shiga-like toxins (i.e. verotoxin) producing *Escherichia coli* infection in humans and pigs. Antibiotics actually enhance toxin production by the bacteria. Therefore, their use increases the risk of developing complications such as HUS. Column 2, lines 39-56. Krivan et al also teach the assembly of various reagents into a diagnostic kit. See column 7, lines 10-16.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the device of Kouvonen to include detection of analytes such as verotoxin or verotoxin-producing *Escherichia coli* because Kouvonen teaches that their device provides the advantages of a simple test that can be performed anywhere and can be adapted for almost any type of analytes; and Williams and Krivan teach that the detection of verotoxin and verotoxin producing *Escherichia coli* is important because these toxins cause significant intestinal bleeding in mammals including humans. A skilled artisan would have had a reasonable expectation of success and would have been motivate to use the device of Kouvonen to detect human hemoglobin and at least verotoxin or verotoxin producing *Escherichia coli* because Krivan teaches that it is important to identify specifically which bacteria causes the symptoms observed because in some instances, standard treatment such as antibiotics, are contraindicated. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to detect hemoglobin along with either verotoxin or verotoxin producing *Escherichia coli* in the same sample because this would provide the advantage of further confirming a diagnosis of possible early onset of HUS caused by verotoxin or verotoxin producing *Escherichia coli,* thus enabling better treatment actions for the disease.

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to assemble the device of Kouvonen as modified by Williams and Krivan into kits such as taught by Krivan for the advantages of convenience and economy.

Response to Arguments

5. Applicant's arguments filed 13 December 2004 have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Kouvonen is limited to the design of a test strip and lack any discussion of detecting any particular type of analyte and that the test strip disclosed by Kouvonen is intended for generic use. Applicant argues that Kouvonen does not teach or refer to the detection of verotoxin or verotoxin producing E. coli and does not allude to testing for these two substances together on the same test strip.

These arguments have been fully considered but are not persuasive. It is true that Kouvonen teaches a test strip that is intended for generic and it is also true that Kouvonen does not specifically disclose the detection of verotoxin or verotoxin producing E. coli; however, contrary to Applicant's arguments, Kouvonen does teach the detection of specific analytes such as hemoglobin (on of the analyte of the instant claims), Salmonella and hormones etc. Kouvonen specifically teaches that their test strip is useful for detecting multiple analytes at the same time, either using the same test strip, or having multiple test strip banded together.

Kouvonen is cited for their teaching that it is possible and well known in the art to use a test strip to simultaneously detect at least two different analytes. The discussion of assays for verotoxin and verotoxin producing E. coli is discussed in both Williams and Krivan.

Applicant argues that Williams does not show or suggest the detection of verotoxin together with the simultaneous detection of the bacterium that produces the verotoxin and that the solid support taught by Williams are cartridges, columns, beads, etc. and does not provide motivation for using the test strip of Kouvonen. In particular, applicant argues that neither reference provides the impetus to simultaneously detect verotoxin and the bacterium that produces it.

Applicant also argues that Krivan does not teach that detection of a combination of toxin and the bacteria that produces it be possible for advantageous. Applicant argues that Krivan only teaches antibody to the toxin and even though Krivan teaches detecting the presence or concentration of toxin and the toxin-producing bacterial, Krivan, in fact does not teach an antibody that can detect the pathogen.

These arguments are not persuasive. Kouvonen teaches a test strip for simultaneously detecting at least two different analytes, one of which is hemoglobin. Williams teaches that it is possible to detect a bacterial toxin, i.e. verotoxin, and provides the reagents for doing so. Krivan, as acknowledged by applicant, teaches the detection of both, the verotoxin and the toxin-producing bacteria.

Therefore, it would have been obvious to one of ordinary skill in the art to modify the device of Kouvonen to include detection of analytes such as verotoxin or verotoxin-producing *Escherichia coli* because Kouvonen teaches that their device provides the advantages of a simple test that can be performed anywhere and can be adapted for almost any type of analytes; and

Williams and Krivan teach that the detection of both, verotoxin and verotoxin producing *Escherichia coli* is important because these toxins cause significant intestinal bleeding in mammals including humans. A skilled artisan would have had a reasonable expectation of success and would have been motivate to use the device of Kouvonen to detect human hemoglobin and at least verotoxin or verotoxin producing *Escherichia coli* because Krivan teaches that it is important to identify specifically which bacteria causes the symptoms observed because in some instances, standard treatment such as antibiotics, are contraindicated. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to detect hemoglobin along with either verotoxin or verotoxin producing *Escherichia coli* in the same sample because this would provide the advantage of further confirming a diagnosis of possible early onset of HUS caused by verotoxin or verotoxin producing *Escherichia coli*, thus enabling better treatment actions for the disease.

The argument that the antibody taught by Krivan does not detect the pathogen is not persuasive since there is no evidence that such is true. Krivan specifically teaches that the presence of toxin-producing bacteria can be detected using the reagents disclosed (column 6, lines 52-63. Krivan also teaches that antibodies that bind to the pathogens and their toxins can be made using methods known in the art (column 3, lines 10-24). Therefore, one of ordinary skill in the art can have a reasonable expectation of success in using the reagents taught by Krivan to detect both the toxin and the toxin-producing pathogen.

The argument that both Williams and Krivan supply teachings regarding the production of antibodies for the detection of verotoxin alone is not persuasive. As discussed above, Krivan specifically teaches the detection of toxin and toxin-producing bacteria (Krivan, column 6, lines 52-63 and claim 11). Krivan also teaches that antibodies recovered from animals inoculated

with various pathogens and their toxins binds to the pathogens and their toxins, and that these antibodies have been used to treat infections in humans and animals caused by the pathogens (Krivan, column 3, lines 10-24).

Applicant argues that there is no suggestion that the methods of Krivan should be carried with a test strip such as that taught by Kouvonen because the preferred embodiment described by Krivan is an ELISA. This argument is not persuasive. Krivan specifically teaches the solid support may be any insoluble material to which the receptors can be found and which may be conveniently used the assay. Substrates such as permeable and semi-permeable membranes are included along with beads. Kouvonen specifically teaches that the use of test strips to detect a wide variety of analytes are well known in the art (see Kouvonen, columns 2 and 3) and specifically, their test strip provides the advantage of a simple and advantageous device which a rapid, sensitive and reliable. Kouvonen teaches that their device provides the advantages of a simple test that can be performed anywhere and can be adapted for almost any type of analytes. Therefore, one of ordinary skill in the art would have been motivated to modify the device of Kouvonen to include detection of analytes such as verotoxin or verotoxin-producing *Escherichia coli* because Williams and Krivan teach that the detection of verotoxin and verotoxin producing *Escherichia coli* is important because these toxins cause significant intestinal bleeding in mammals including humans, and that in certain instances antibiotics are contraindicated in the treatment of toxin-producing E. coli infection, therefore, it is important to accurately detect the specific pathogens as well as their toxin (Krivan, column 2, lines 39-50).

Applicant argues that the instant invention provides a convenient and simply way to detect a combination of at least two of verotoxin-producing E. coli, verotoxin, and human hemoglobin and submitted, as Exhibit I, the results of applying the assay kit to clinical isolates.

The results purported to show the detection of E. coli and/or verotoxin, and/or hemoglobin which may be present without concurrent infection.

These results have been fully considered but are not persuasive. It is noted that the arguments regarding the exhibit is directed toward assay kits which are not claimed. The instant claims are drawn to method for detecting, as such, the various assay steps and reagents have not been fully disclosed in the exhibit. Furthermore, the exhibit does not show any unexpected or improved results. It seems that the results obtain by Applicant would be fully expected by one of ordinary skill in the art using the test strip of Kouvonen as modified by Williams and Krivan to detect verotoxin and either the toxin-producing bacteria or hemoglobin.

Conclusion

6. No claim is allowed.

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 8:00 a.m. -3:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641
1/17/05